UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/729,895	12/05/2003	Cheryl L. Willman	N12-038US	2100

28156 7590 09/07/2006

COLEMAN SUDOL SAPONE, P.C.
714 COLORADO AVENUE
BRIDGE PORT, CT 06605-1601

EXAMINER	
GODDARD, LAURA B	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 09/07/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/729,895	WILLMAN ET AL.	
	Examiner	Art Unit	
	Laura B. Goddard, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *1* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 October 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-78* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-78* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

1. Claims 1-3, 7, 8, 14, 15, drawn to an isolated OPAL1 polynucleotide and a pharmaceutical composition comprising a polynucleotide of claim 1, classified in class 536, subclass 23.1.

Additionally, Applicants must elect a single OPAL1 splice variant nucleic acid sequence SEQ ID NO: 1 or 3 and the corresponding encoded protein SEQ ID NO:2 or 4 as each sequence presents a structurally and functionally *distinct* invention not a species.

2. Claims 4-6, 14, 15, drawn to an isolated OPAL1 polypeptide and a pharmaceutical composition comprising a polypeptide of claim 4, classified in class 530, subclass 350.

Additionally, Applicants must elect a single OPAL1 splice variant amino acid sequence SEQ ID NO: 2 or 4 as each sequence presents a structurally and functionally *distinct* invention not a species.

3. Claims 9, 43, drawn to an isolated antibody or antigen binding fragment thereof that specifically binds to the polypeptide of claim 4 or 5, classified in class 530, subclass 387.1.

Additionally, Applicants must elect a single OPAL1 splice variant amino acid sequence SEQ ID NO: 2 or 4 to which the antibody binds as each sequence presents a structurally and functionally *distinct* invention not a species.

4. Claims 10, 11, 60-65, drawn to a method for predicting therapeutic outcome in a leukemia patient comprising determining the expression level for an OPAL1 gene product to yield an observed OPAL 1 gene expression level and comparing the observed OPAL1 gene expression level to a control OPAL1 gene expression level, wherein the **OPAL1 protein expression level is measured;** said method further comprising determining the expression level for a G1 product to yield an observed G1 or G2 gene expression level and comparing the observed G1 or G2 expression level for the G2 or G2 gene product to a control G1 or G2 gene expression level, wherein the **G1 or G2 gene protein expression level is measured**, classified in class 435, subclass 7.1.

Additionally, Applicants must elect a single OPAL1 splice variant amino acid sequence SEQ ID NO: 2 or 4 as each sequence presents a structurally and functionally *distinct* invention not a species.

Additionally, Applicants must elect a single gene expression product G1 or G2 as each product presents a structurally and functionally *distinct* invention not a species.

5. Claims 10, 11, 60-65, drawn to a method for predicting therapeutic outcome in a leukemia patient comprising determining the expression level for an OPAL1 gene product to yield an observed OPAL 1 gene expression level and comparing the observed OPAL1 gene expression level to a control OPAL1 gene expression level, wherein the **OPAL1 protein expression level is measured;** said method further comprising

determining the expression level for a G1 product to yield an observed G1 or G2 gene expression level and comparing the observed G1 or G2 expression level for the G2 or G2 gene product to a control G1 or G2 gene expression level, wherein the **G1 or G2 gene mRNA expression level is measured**, classified in class 435, subclasses 7.1, 6.

Additionally, Applicants must elect a single OPAL1 splice variant amino acid sequence SEQ ID NO: 2 or 4 as each sequence presents a structurally and functionally *distinct* invention not a species.

Additionally, Applicants must elect a single gene expression product G1 or G2 as each product presents a structurally and functionally *distinct* invention not a species.

6. Claims 10, 11, 60-65, drawn to a method for predicting therapeutic outcome in a leukemia patient comprising determining the expression level for an OPAL1 gene product to yield an observed OPAL 1 gene expression level and comparing the observed OPAL1 gene expression level to a control OPAL1 gene expression level, wherein the OPAL1 **mRNA expression level is measured;** said method further comprising determining the expression level for a G1 product to yield an observed G1 or G2 gene expression level and comparing the observed G1 or G2 expression level for the G2 or G2 gene product to a control G1 or G2 gene expression level, wherein the **G1 or G2 gene protein expression level is measured**, classified in class 435, subclasses 7.1, 6.

Additionally, Applicants must elect a single OPAL1 splice variant nucleotide sequence SEQ ID NO: 1 or 3 as each sequence presents a

structurally and functionally *distinct* invention not a species. (see additional requirement next page)

Additionally, Applicants must elect a single gene expression product G1 or G2 as each product presents a structurally and functionally *distinct* invention not a species.

7. Claims 10, 11, 60-65, drawn to a method for predicting therapeutic outcome in a leukemia patient comprising determining the expression level for an OPAL1 gene product to yield an observed OPAL 1 gene expression level and comparing the observed OPAL1 gene expression level to a control OPAL1 gene expression level, wherein the OPAL1 **mRNA expression level is measured;** said method further comprising determining the expression level for a G1 product to yield an observed G1 or G2 gene expression level and comparing the observed G1 or G2 expression level for the G2 or G2 gene product to a control G1 or G2 gene expression level, wherein the **G1 or G2 gene mRNA expression level is measured**, classified in class 435, subclass 6.

Additionally, Applicants must elect a single OPAL1 splice variant nucleotide sequence SEQ ID NO: 1 or 3 as each sequence presents a structurally and functionally *distinct* invention not a species.

Additionally, Applicants must elect a single gene expression product G1 or G2 as each product presents a structurally and functionally *distinct* invention not a species.

8. Claim 12, drawn to a method for detecting an OPAL1 **polynucleotide** in a biological sample comprising contacting the sample with the

polynucleotide of claim 1 for hybridization to an OPAL1 gene, classified in class 435, subclass 6.

Additionally, Applicants must elect a single OPAL1 splice variant nucleotide sequence SEQ ID NO: 1 or 3, as each sequence presents a structurally and functionally *distinct* invention not a species.

9. Claim 13, drawn to a method for detecting an OPAL1 **protein** in a biological sample comprising contacting the sample with an antibody that binds to the polypeptide of claim 4, classified in class 435, subclass 7.1.

Additionally, Applicants must elect a single OPAL1 splice variant amino acid sequence SEQ ID NO: 2 or 4, as each sequence presents a structurally and functionally *distinct* invention not a species.

10. Claims 14 and 15, drawn to a pharmaceutical composition comprising a compound that enhances the activity of the polypeptide of claim 4, classified in class 424, subclass 1.11.

Additionally, Applicants must elect a single OPAL1 splice variant amino acid sequence SEQ ID NO: 2 or 4, as each sequence presents a structurally and functionally *distinct* invention not a species.

11. Claims 16 and 17, drawn to a method for treating leukemia comprising administering to a leukemia patient a therapeutic agent that increases the amount or activity of the polypeptide of claim 4 in the patient; said method further comprising administering an agent that alters the amount or activity of a G1 or G2 polypeptide, classified in class 514, subclass 2.

Additionally, Applicants must elect a single OPAL1 splice variant amino acid sequence SEQ ID NO: 2 or 4, as each sequence presents a structurally and functionally *distinct* invention not a species.

Additionally, Applicants must elect G1 or G2 as the polypeptide in which the amount or activity is altered by an agent, as each agent that alters a distinct polypeptide presents a structurally and functionally *distinct* invention not a species.

12. Claims 18, 19, 66-68, drawn to an ***in vitro*** method for screening compounds useful for treating leukemia comprising: determining the expression level for an OPAL1 gene product in a cell culture prior to contact with a candidate compound and determining the expression level for the OPAL1 gene product in the cell culture after contact with the candidate compound; said method further comprising determining the expression level for a G1 gene product or both G1 and G2 gene product in cell culture; and **wherein the OPAL1, G1 and G2 gene product expression level measured are proteins**, classified in class 435, subclass 7.1.

Additionally, Applicants must elect a single OPAL1 splice variant amino acid sequence SEQ ID NO: 2 or 4, as each sequence presents a structurally and functionally *distinct* invention not a species.

13. Claims 18, 19, 66-68, drawn to an ***in vitro*** method for screening compounds useful for treating leukemia comprising: determining the expression level for an OPAL1 gene product in a cell culture prior to contact with a candidate compound and determining the expression level for the OPAL1 gene product in the cell culture after contact with the

candidate compound; said method further comprising determining the expression level for a G1 gene product or both G1 and G2 gene product in cell culture; and **wherein the OPAL1, G1 and G2 gene product expression level measured are mRNA**, classified in class 435, subclass 6.

Additionally, Applicants must elect a single OPAL1 splice variant nucleotide sequence SEQ ID NO: 1 or 1, as each sequence presents a structurally and functionally *distinct* invention not a species.

14. Claims 20, 69-73, drawn to an ***in vivo*** method for evaluating a compound for use in treating leukemia comprising obtaining a first biological sample from a patient, determining the expression level for an OPAL1 gene product in the first sample prior to administration of a candidate compound, administering the compound to the patient, obtaining a second biological sample, and determining the expression level for an OPAL1 gene product in the second biological sample; said method further comprising determining the expression level for a G1 gene product or both G1 and a G2 gene product; **wherein the OPAL1, G1 and G2 gene product expression level measured are protein**, classified in class 424, subclass 9.2.

Additionally, Applicants must elect a single OPAL1 splice variant amino acid sequence SEQ ID NO: 2 or 4, as each sequence presents a structurally and functionally *distinct* invention not a species.

NOTE: It appears claim 71 is supposed to depend on claim 20, not claim 18 because of lack of antecedent basis for "biological sample" with dependency on claim 18, hence claim 71 was included in Group 14.

15. Claims 20, 69-73, drawn to an ***in vivo*** method for evaluating a compound for use in treating leukemia comprising obtaining a first biological sample from a patient, determining the expression level for an OPAL1 gene product in the first sample prior to administration of a candidate compound, administering the compound to the patient, obtaining a second biological sample, and determining the expression level for an OPAL1 gene product in the second biological sample; said method further comprising determining the expression level for a G1 gene product or both a G1 and a G2 gene product; **wherein the OPAL1, G1 and G2 gene product expression level measured are mRNA**, classified in class 424, subclass 9.2.

Additionally, Applicants must elect a single OPAL1 splice variant nucleotide sequence SEQ ID NO: 1 or 3, as each sequence presents a structurally and functionally *distinct* invention not a species.

NOTE: It appears claim 71 is supposed to depend on claim 20, not claim 18 because of lack of antecedent basis for "biological sample" with dependency on claim 18, hence claim 71 was included in Group 15.

16. Claims 21-26, 44-51, drawn to a method for classifying leukemia in a patient comprising obtaining a biological sample form a patient, determining the **expression level for a selected gene product** to yield an observed gene expression level, and comparing the observed gene expression level for the selected gene product to a control gene

expression level, **wherein the expression level of the protein is measured**, classified in class 424, subclass 9.1.

17. Claims 21-26, 44-51, drawn to a method for classifying leukemia in a patient comprising obtaining a biological sample form a patient, determining the **expression level for a selected gene product** to yield an observed gene expression level and comparing the observed gene expression level for the selected gene product to a control gene expression level, **wherein the expression level of mRNA is measured**, classified in class 424, subclass 9.1.

18. Claims 27-32, 52-59, drawn to a method for classifying leukemia in a patient comprising obtaining a biological sample from a patient, determining a **gene expression profile** for selected gene products that correlates with a disease classification; wherein a similarity between the observed gene expression profile and the control gene expression profile is indicative of the disease classification; **wherein the expression level of the protein is measured**, classified in class 424, subclass 9.1.

19. Claims 27-32, 52-59, drawn to a method for classifying leukemia in a patient comprising obtaining a biological sample from a patient,

determining a **gene expression profile** for selected gene products that correlates with a disease classification; wherein a similarity between the observed gene expression profile and the control gene expression profile is indicative of the disease classification; **wherein the expression level of the mRNA is measured**, classified in class 424, subclass 9.1.

20. Claims 33-36, 74, 75, drawn to an ***in vitro*** method for screening compounds useful for treating acute leukemia comprising determining the expression level for a selected gene product(s) in a cell culture to yield an observed expression level for the gene product(s) prior to contact with a candidate compound, wherein the selected gene product(s) is correlated with therapeutic outcome, contacting the cell culture with a candidate compound, determining the expression level for the selected gene product(s) in a cell culture to yield an observed gene expression level after contact with the candidate compound, wherein a modulation of gene expression level after contact with the compound is indicative of therapeutic utility, **and wherein the expression level of the protein is measured**, classified in class 435, subclass 7.1.

21. Claims 33-36, 74, 75, drawn to an ***in vitro*** method for screening compounds useful for treating acute leukemia comprising determining the expression level for a selected gene product(s) in a cell culture to yield an

observed expression level for the gene product(s) prior to contact with a candidate compound, wherein the selected gene product(s) is correlated with therapeutic outcome, contacting the cell culture with a candidate compound, determining the expression level for the selected gene product(s) in a cell culture to yield an observed gene expression level after contact with the candidate compound, wherein a modulation of gene expression level after contact with the compound is indicative of therapeutic utility, **and wherein the expression level of the mRNA is measured**, classified in class 435, subclass 6.

22. Claims 37-40, 76, 77, drawn to an ***in vitro*** method for screening compounds useful for treating acute leukemia comprising contacting an experimental cell culture with a candidate compound, determining the expression level for a selected gene product(s) in the cell culture to yield an experimental gene expression level for the gene product(s), wherein the selected gene product(s) is correlated with therapeutic outcome, comparing the experimental gene expression level to the expression level of the selected gene product(s) in a control cell culture, wherein a relative difference in the gene expression levels between the experimental and control cultures is indicative of therapeutic utility; **and wherein the expression level of the protein is measured**, classified in class 435, subclass 7.1.

23. Claims 37-40, 76, 77, drawn to an ***in vitro*** method for screening compounds useful for treating acute leukemia comprising contacting an experimental cell culture with a candidate compound, determining the expression level for a selected gene product(s) in the cell culture to yield an experimental gene expression level for the gene product(s), wherein the selected gene product(s) is correlated with therapeutic outcome, comparing the experimental gene expression level to the expression level of the selected gene product(s) in a control cell culture, wherein a relative difference in the gene expression levels between the experimental and control cultures is indicative of therapeutic utility **and wherein the expression level of the mRNA is measured**, classified in class 435, subclass 6.

24. Claims 41, 42, 78, drawn to an ***in vivo*** method for evaluating a compound for use in treating leukemia comprising obtaining a first biological sample from a patient, determining a gene expression profile for selected gene products to yield an observed gene expression profile prior to administration of a candidate compound, wherein the selected gene products are correlated with therapeutic outcome, administering a candidate compound to the patient, obtaining a second biological sample, determining a gene expression profile for the selected gene products in

the second sample to yield an observed gene expression profile after administration of the candidate compound; and comparing the observed gene expression profiles before and after administration of the candidate compound to determine whether the compound has therapeutic utility; **and wherein the protein expression is measured**, classified in class 435, subclass 7.1.

25. Claims 41, 42, 78, drawn to an ***in vivo*** method for evaluating a compound for use in treating leukemia comprising obtaining a first biological sample from a patient, determining a gene expression profile for selected gene products to yield an observed gene expression profile prior to administration of a candidate compound, wherein the selected gene products are correlated with therapeutic outcome, administering a candidate compound to the patient, obtaining a second biological sample, determining a gene expression profile for the selected gene products in the second sample to yield an observed gene expression profile after administration of the candidate compound; and comparing the observed gene expression profiles before and after administration of the candidate compound to determine whether the compound has therapeutic utility; **and wherein the mRNA expression is measured**, classified in class 435, subclass 6.

The inventions are distinct, each from the other because of the following reasons:

The DNA of Group 1 is related to the protein of Group 2 by virtue of the fact that the DNA codes for the protein. The DNA molecule has utility for the recombinant production of the protein in a host cell. Although the DNA and the protein are related, since the DNA encodes the specifically claimed protein, they are distinct inventions because the protein product can be made by other and materially distinct processes, such as purification from the natural source. Further, DNA can be used for processes other than the production of protein, such as nucleic acid hybridization assays.

Furthermore, searching the inventions of Groups 1 and 2 together would impose a serious search burden. In the instant case, the search of the polypeptides and polynucleotides are not coextensive. The inventions of Groups 1 and 2 have a separate status in the art as shown by their different classifications. In cases such as this one where descriptive sequence information is provided, the sequences are searched in appropriate database. There is search burden also in the non-patent literature. Prior to the concomitant isolation and expression of the sequences of interest there may be journal articles devoted solely to polypeptides which would not have described the polynucleotide. Similarly, there may have been "classical" genetics papers which had no knowledge of the polypeptide but spoke to the gene. Searching, therefore is not coextensive. This search requires an extensive analysis of the art retrieved in a sequence search and will require an in-depth analysis of technical literature. The scope of polynucleotides as claimed extend beyond the polynucleotide that encodes the claimed polypeptides as explained above, furthermore, a search of the nucleic acid

molecules of Group 1 would require an oligonucleotide search, which is not likely to result in relevant art with respect to the polypeptide of Group 2. As such, it would be burdensome to search the inventions of Groups 1 and 2.

The polypeptide of Group 2 and the antibody of Group 3 are patentably distinct for the following reasons:

While the inventions of both Group 2 and Group 3 are polypeptides, in this instance the polypeptides of Group 2 represent various proposed cell cycling protein, whereas the polypeptide of Group 3 encompasses antibodies including IgG which comprises 2 heavy and 2 light chains containing constant and variable regions, and including framework regions which act as a scaffold for the 6 complementarily determining regions (CDR) that function to bind an epitope. Thus the polypeptides of Group 2 and the antibodies of Group 3 are structurally distinct molecules; any relationship between a polypeptide of Group 2 and an antibody of Group 3 is dependent upon the correlation between the scope of the polypeptides that the antibody binds and the scope of the antibodies that would be generated upon immunization with the polypeptide.

In this case, the polypeptides of group 2 encompass large molecules which contain potentially hundreds of regions to which an antibody may bind, whereas the antibody of Group 3 is defined in terms of its binding specificity to a small structure within the sequences encompassed by Group 2. Furthermore, searching the inventions of Group 2 and Group 3 would impose a serious search burden. The inventions have separate status in the art as shown by their different classifications. A polypeptide and

an antibody which binds to the polypeptide require different searches. An amino acid sequence search of the full-length protein is necessary for a determination of novelty and unobviousness of the protein. However, such a search is not required to identify the antibodies of Group 3. Furthermore, antibodies which bind to an epitope of a polypeptide of Group 2 may be known even if a polypeptide of Group 2 is novel. In addition, the technical literature search for the polypeptides of Group 2 and the antibody of Group 3 are not coextensive, e.g., antibodies may be characterized in the technical literature prior to discovery of or sequence of their binding target.

The polynucleotide of Group 1 and the antibody of Group 3 are patentably distinct for the following reasons:

The antibody of Group 3 includes, for example, IgG molecules which comprise 2 heavy and 2 light chains containing constant and variable regions, and including framework regions which act as a scaffold for the 6 complementarily determining regions (CDRs). Polypeptides, such as the antibody of Group 3 which are composed of amino acids, and polynucleotides, which are composed of nucleic acids, are structurally distinct molecules; any relationship between a polynucleotide and polypeptide is dependent upon the information provided by nucleic acid sequence open reading frame as it corresponds to the primary amino acid sequence of the encoded polypeptide. In the present claims, a polynucleotide of Group 1 will not encode an antibody of Group 3, and the antibody of Group 3 cannot be encoded by a polynucleotide of Group 1. Therefore, the antibody and polynucleotide are patentably distinct.

The antibody and polynucleotide inventions have a separate status in the art as shown by their different classifications. Furthermore, searching the inventions of Group 1 and Group 3 would impose a serious search burden since a search of the polynucleotides of Group 1 would not be used to determine the patentability of any antibody of Group 3, and vice-versa.

The product of Group 10, a pharmaceutical composition comprising a compound that enhances the activity of the polypeptide of Group 2, is structurally and functionally distinct from the products of Groups 1-3. A search of the product of Group 10 would not be coextensive with a search of the products of Groups 1-2 and would invoke a high burden of search.

The inventions of Groups 4-9 and 11-25 are materially distinct methods which differ at least in objectives, method steps and/or reagents. For example, Groups 4-7 are drawn to a method for predicting therapeutic outcome in a leukemia patient, however each Group comprises measuring structurally and functionally distinct molecules which require different method steps and reagents. Group 8 is drawn to the different objective of detecting an OPAL1 polynucleotide. Group 9 is drawn to the different objective of detecting an OPAL1 protein. Group 11 is drawn to the different objective of treating leukemia in a patient. Groups 12 and 13 are drawn to the different objective of and *in vitro* method for screening for compounds useful for treating leukemia however each Group comprises distinct methods steps, reagents, and measure structurally and functionally distinct OPAL1 protein expression or mRNA expression. Groups 14 and 15 are drawn to the different objective of an *in vivo* method for evaluating a compound for

use in treating leukemia, wherein each Group comprises distinct methods steps, reagents, and measure structurally and functionally distinct OPAL1 protein expression or mRNA expression. Groups 16-19 are drawn to the different objective of classifying leukemia in a patient wherein each Group comprises distinct methods steps, reagents, determining a gene expression profile or the expression level for a selected gene product(s), and measure structurally and functionally distinct OPAL1 protein expression or mRNA expression. Groups 20-23 are drawn to an *in vitro* method for screening compounds useful for treating acute leukemia however each Group comprises different method steps and measure structurally and functionally distinct OPAL1 protein expression or mRNA expression. Groups 24 and 25 are drawn to the different objective of an *in vivo* method for screening compounds useful for treating acute leukemia, wherein each Group comprises distinct method steps, reagents, and measure structurally and functionally distinct OPAL1 protein expression or mRNA expression. Each of the groups employs chemically distinct reagents to accomplish same or different objectives that comprise different method steps, reagents and/or dosages and/or schedules used, response variables, and criteria for success. Searching all of the groups with all of the different variables would invoke a high burden of search.

Inventions 3 and 4, 5, 9, 12, 14, 16, 18, 20, 22, 24 are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product. See MPEP § 806.05(h). In

the instant case the antibody of Group 3 can be used to produce anti-idiotypic antibodies or for affinity chromatography.

Inventions 10 and 11 are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product. See MPEP § 806.05(h). In the instant case the compound of Group 10 can be used in *in vitro* assays or for affinity chromatography.

The product of Group 1 is not used in the methods of Groups 4-9 and 11-25. The product of Group 2 is not used in the methods of Groups 4-9 and 11-25. The product of Group 3 is not used in the methods of Groups 6-8, 11, 13, 15, 17, 19, 21, 23, and 25. The product of Group 10 is not used in the methods of Groups 4-9 and 12-25.

Because these inventions are distinct for the reasons given above and the search required for one Group is not required for any other Group, and because some Groups have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper.

Note:

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and the product claims are subsequently found allowable, withdrawn process claims that depend from or otherwise require all the limitations of the allowable product claim will be considered for rejoinder. All claims directed a nonelected process invention must require all the limitations of an allowable product claim for that process invention to be rejoined.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process

claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103 and 112. Until all claims to the elected product are found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowable product claim will not be rejoined. See MPEP § 821.04(b). Additionally, in order to retain the right to rejoinder in accordance with the above policy, applicant is advised that the process claims should be amended during prosecution to require the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder**. Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

SPECIES ELECTION

Species election for Group 10

A. This application contains claims directed to the following patentably distinct species of second therapeutic target (claim 15): **(i) polynucleotide encoding G1, (i) polynucleotide encoding G2, (ii) a G1 polypeptide, (ii) a G2 polypeptide, (iii) a compound that alters the activity of a G1 polypeptide, or (iii) a compound that alters the activity of a G2 polypeptide.** The species are independent or distinct because each second therapeutic is a structurally and functionally distinct molecule.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claim 14 is generic.

Species election for Groups 16 and 17

B. This application contains claims directed to the following patentably distinct species of disease classification: **comprising predicted remission (claim 22), comprising therapeutic failure (claim 22), based on karyotype (claim 24), comprising leukemia subtype (claim 25), or based on disease etiology (claim 26).** The species are independent or distinct because each disease classification comprises distinct method steps requiring different reagents, response variables, and criteria for success.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claim 21 is generic.

If Applicant elects species of "predicted remission" or "therapeutic failure" from B above, Applicant must elect a species from C below:

C. This application contains claims directed to the following patentably distinct species of genes: **OPAL1 (SEQ ID NO:1), OPAL1 (SEQ ID NO:3), G1, G2, FYN binding protein, PBK1, osteonectin or a gene listed in Tables 4-12, 15-18, 20, 24, 29-42, 47, or 53-57.** The species are independent or distinct because each gene produces a structurally and functionally distinct product.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claims 21 and 22 are generic.

If Applicant elects the species of classification "based on karyotype" in B above, Applicant must elect a species from D below:

D. This application contains claims directed to the following patentably distinct species of gene: **one gene from Table 13, 14, 21, 26, 27, Figure 8, 14, 16, 17, or 18 (claim 44), Table 51 or 52 (claim 46), or Figure 7 (claim 48). The species are independent or distinct because each gene produces a structurally and functionally distinct product.** Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claims 21 and 24 are generic.

If Applicant elects the species of classification "based on disease etiology" in B above, Applicant must elect a species from E below:

E. This application contains claims directed to the following patentably distinct species of gene: **one gene from Table 43 (claims 49 and 50), Table 45, 58-60, or Figure 15 (claims 49 and 51).** The species are independent or distinct because each gene produces a structurally and functionally distinct product. Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claims 21 and 26 are generic.

Species election for Groups 18 and 19

F. This application contains claims directed to the following patentably distinct species of disease classification: **comprising predicted remission (claim 28), comprising therapeutic failure (claim 28), based on karyotype (claim 30), comprising leukemia subtype (claim 31), or based on disease etiology (claim 32).** The species are independent or distinct because each disease classification comprises distinct method steps requiring different reagents, response variables, and criteria for success.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claim 27 is generic.

If Applicant elects species of "predicted remission" or "therapeutic failure" from F above, Applicant must elect a species from G below:

G. This application contains claims directed to the following patentably distinct species of genes (claim 29): **OPAL1 (SEQ ID NO:1), OPAL1 (SEQ ID NO:3), G1, G2, FYN binding protein, PBK1, osteonectin or a gene listed in Tables 4-12, 15-18, 20, 24, 29-42, 47, or 53-57.** The species are independent or distinct because each gene produces a structurally and functionally distinct product.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claims 27 and 28 are generic.

If Applicant elects the species of classification "based on karyotype" in F above, Applicant must elect a species from H below:

H. This application contains claims directed to the following patentably distinct species of gene: **one gene from Table 13, 14, 21, 26, 27, Figure 8, 14, 16, 17, or 18 (claim 52). The species are independent or distinct because each gene produces a structurally and functionally distinct product.** Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claims 27 and 30 are generic.

If Applicant elects the species of classification "comprises leukemia subtype" in F above, Applicant must elect a species from I below:

I. This application contains claims directed to the following patentably distinct species of gene: **one gene from Table 51 or 52 (claim 54), or Figure 7 (claim 56). The species are independent or distinct because each gene produces a structurally and functionally distinct product.** Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claims 27 and 31 are generic.

If Applicant elects the species of classification "based on disease etiology" in F above, Applicant must elect a species from J below:

J. This application contains claims directed to the following patentably distinct species of gene: **one gene from Table 43 (claims 57 and 58), Table 45, 58-60, or Figure 15 (claims 57 and 59).** The species are independent or distinct because each gene produces a structurally and functionally distinct product. Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claims 27 and 32 are generic.

Species election for Groups 20 and 21

K. This application contains claims directed to the following patentably distinct species of genes (claim 34 and 36): **OPAL1 (SEQ ID NO:1), OPAL1 (SEQ ID NO:3), G1, G2, FYN binding protein, PBK1, osteonectin or a gene listed in Tables 4-12, 15-18, 20, 24, 29-42, 47, or 53-57.** The species are independent or distinct because each gene produces a structurally and functionally distinct product.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claim 33 is generic.

If Applicant elects the species of gene "OPAL1 (SEQ ID NO:1)" or "OPAL1 (SEQ ID NO:3)" in K above, Applicant must elect a species from L below:

L. This application contains claims directed to the following patentably distinct species of additional gene (claims 74 and 75): **G1 or both G1 and G2.** The species are

independent or distinct because each gene produces a structurally and functionally distinct product. Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claims 33 and 35 are generic.

Species election for Groups 22 and 23

M. This application contains claims directed to the following patentably distinct species of genes (claim 38 and 40): **OPAL1 (SEQ ID NO:1), OPAL1 (SEQ ID NO:3), G1, G2, FYN binding protein, PBK1, osteonectin or a gene listed in Tables 4-12, 15-18, 20, 24, 29-42, 47, or 53-57.** The species are independent or distinct because each gene produces a structurally and functionally distinct product.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claims 37 and 39 are generic.

If Applicant elects the species of gene "OPAL1 (SEQ ID NO:1)" or "OPAL1 (SEQ ID NO:3)" in M above, Applicant must elect a species from N below:

N. This application contains claims directed to the following patentably distinct species of additional gene (claims 76 or 77): **G1 or both G1 and G2.** The species are independent or distinct because each gene produces a structurally and functionally distinct product. Applicant is required under 35 U.S.C. 121 to elect a single disclosed

species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claims 37 and 39 are generic.

Species election for Groups 24 and 25

O. This application contains claims directed to the following patentably distinct species of genes (claim 42): **OPAL1 (SEQ ID NO:1), OPAL1 (SEQ ID NO:3), G1, G2, FYN binding protein, PBK1, osteonectin or a gene listed in Tables 4-12, 15-18, 20, 24, 29-42, 47, or 53-57.** The species are independent or distinct because each gene produces a structurally and functionally distinct product.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claim 41 is generic.

If Applicant elects the species of gene "OPAL1 (SEQ ID NO:1)" or "OPAL1 (SEQ ID NO:3)" in O above, Applicant must elect a species from P below:

P. This application contains claims directed to the following patentably distinct species of additional gene (claim 78): **G1 or both G1 and G2.** The species are independent or distinct because each gene produces a structurally and functionally distinct product. Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claim 41 is generic.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Since the decisions in *In re Weber*, 580 F.2d 455, 198 USPQ 328 (CCPA 1978) and *In re Haas*, 580 F.2d 461, 198 USPQ 334 (CCPA 1978), it is improper for the Office to refuse to examine that which applicants regard as their invention, unless the subject matter in a claim lacks unity of invention. *In re Harnisch*, 631 F.2d 716, 206 USPQ 300 (CCPA 1980); and *Ex parte Hozumi*, 3 USPQ2d 1059 (Bd. Pat. App. & Int. 1984). Broadly, unity of invention exists where compounds included within a Markush group (1) share a common utility, and (2) share a substantial structural feature essential to that utility.

Applicant is advised that the reply to this requirement to be complete must include (i) an election of a species or invention to be examined even though the

requirement be traversed (37 CFR 1.143) and (ii) identification of the claims encompassing the elected invention.

The election of an invention or species may be made with or without traverse. To reserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the restriction requirement, the election shall be treated as an election without traverse.

Should applicant traverse on the ground that the inventions or species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the inventions or species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C.103(a) of the other invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Laura B. Goddard, Ph.D. whose telephone number is (571) 272-8788. The examiner can normally be reached on 8:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Laura B Goddard, Ph.D.
Examiner
Art Unit 1642

JEFFREY SIEW
SUPERVISORY PATENT EXAMINER